Status: Currently Official on 14-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-5EA69836-6C5B-4B36-ABD5-0FC36B44F302_1_en-US
DOI: https://doi.org/10.31003/USPNF_M28355_01_01
DOI Ref: gnu8w

Doxycycline Hyclate Delayed-Release Capsules

DEFINITION

Doxycycline Hyclate Delayed-Release Capsules contain the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$).

IDENTIFICATION

• **A.**

Test solution: Nominally 1 mg/mL of doxycycline in methanol from finely powdered Capsule contents. Pass through a filter, and use the filtrate.

Analysis: Proceed as directed in *Identification—Tetracyclines ⟨193⟩, Method II*.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Mobile phase: Transfer 2.72 g of monobasic potassium phosphate, 0.74 g of sodium hydroxide, 0.50 g of tetrabutylammonium hydrogen sulfate, and 0.40 g of edetate disodium to a 1000-mL volumetric flask. Add 850 mL of water, and stir to dissolve. Add 60 g of tertiary butyl alcohol with the aid of water, dilute with water to volume, and adjust with 1 N sodium hydroxide to a pH of 8.0 ± 0.1. Pass this solution through a filter of 0.5-µm or finer pore size, and degas before using. Decreasing the proportion of tertiary butyl alcohol results in a longer retention time of doxycycline and improved separation of doxycycline from the related compounds.

Diluent: 0.01 N hydrochloric acid

System suitability stock solution: 6 mg/mL of doxycycline from USP Doxycycline Hyclate RS in *Diluent*

System suitability solution: Transfer 5 mL of *System suitability stock solution* to a 25-mL volumetric flask, heat on a steam bath for 60 min, and evaporate to dryness on a hot plate, taking care not to char the residue. Dissolve the residue in 0.01 N hydrochloric acid, and dilute with *Diluent* to volume. Pass a portion of this solution through a filter of 0.5-µm or finer pore size, and use the filtrate. This solution contains a mixture of 4-epidoxycycline, 6-epidoxycycline, and doxycycline. When stored in a refrigerator, this solution may be used for 14 days.

Standard solution: 1.2 mg/mL of USP Doxycycline Hyclate RS in *Diluent*. Sonicate as needed to dissolve. Protect the *Standard solution* from light.

Sample solution: Nominally 1 mg/mL of doxycycline in *Diluent*, prepared as follows. Remove as completely as possible the contents of NLT 20 Capsules. Mix the combined contents, and transfer a suitable portion of the powder to a suitable volumetric flask. Add 75% of the final volume of *Diluent*, sonicate for 5 min, shake for 15 min, and dilute with *Diluent* to volume. Pass through a membrane filter of 0.5-µm or finer pore size.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 270 nm

Column: 4.6-mm × 25-cm; packing L21

Column temperature: 60 ± 1°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: 1.7 times the retention time of doxycycline

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for 4-epidoxycycline (the main degradation product), 6-epidoxycycline, and doxycycline are about 0.4, 0.7, and 1.0, respectively, *System suitability solution*.]

Suitability requirements

Resolution: NLT 3.0 between the 4-epidoxycycline peak and the doxycycline peak, *System suitability solution*

Tailing factor: NMT 2.0 for doxycycline, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times F \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Doxycycline Hyclate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of the *Sample solution* (mg/mL)

P = potency of doxycycline in USP Doxycycline Hyclate RS (µg/mg)

F = conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–120.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩:** Proceed as directed for *Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B, Procedure*.

Acid stage

Conduct the test by transferring the contents of each Capsule to the individual basket units of the apparatus.

Medium: 0.06 N hydrochloric acid; 900 mL

Apparatus 1: 50 rpm

Time: 20 min

Detector: UV 345 nm

Diluent: 0.1 N hydrochloric acid

Standard solution: 10 µg/mL of USP Doxycycline Hyclate RS in *Diluent*

Sample solution: Dilute filtered portions of the solution under test with *Diluent* to a concentration that is similar to the *Standard solution*.

Tolerances

Level 1 (6 Capsules tested): No individual value exceeds 50% dissolved.

Level 2 (6 Capsules tested): NMT 2 individual values of 12 tested are greater than 50% dissolved.

Buffer stage

Conduct this stage of testing on separate specimens, selecting Capsules that were not previously subjected to *Acid stage* testing and transferring the contents of each Capsule to the individual basket units of the apparatus.

Medium: pH 5.5 neutralized phthalate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 1000 mL

Apparatus 1: 50 rpm

Time: 30 min

Detector: UV 345 nm

Diluent: 0.1 N hydrochloric acid

Standard solution: 10 µg/mL of USP Doxycycline Hyclate RS in *Diluent*

Sample solution: Dilute filtered portions of the solution under test with *Diluent* to a concentration that is similar to the *Standard solution*.

Tolerances: NLT 85% (*Q*) of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

SPECIFIC TESTS

• **Water Determination, *Method I*⟨921⟩:** NMT 5.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **Labeling:** The label indicates that the contents of the Capsules are enteric coated.

• **USP Reference Standards ⟨11⟩**

USP Doxycycline Hyclate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
DOXYCYCLINE HYCLATE DELAYED-RELEASE CAPSULES	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 31(1)

Current DocID: GUID-5EA69836-6C5B-4B36-ABD5-0FC36B44F302_1_en-US

DOI: https://doi.org/10.31003/USPNF_M28355_01_01

DOI ref: gnu8w